BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

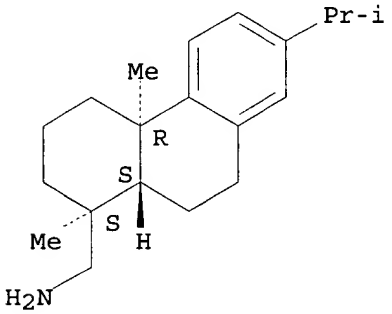
As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

L2 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **77831-62-0** REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo-, (R)-, compd. with [1S-(1.alpha.,4a.beta.,10a.alpha.)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenemethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Phenanthrenemethanamine, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1.alpha.,4a.beta.,10a.alpha.)]-, (R)-6-oxo-2-piperidinecarboxylate (9CI)
FS STEREOSEARCH
MF C20 H31 N . C6 H9 N O3
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 77831-59-5
CMF C20 H31 N

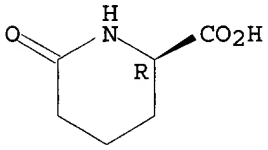
Absolute stereochemistry.



CM 2

CRN 72002-30-3
CMF C6 H9 N O3

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

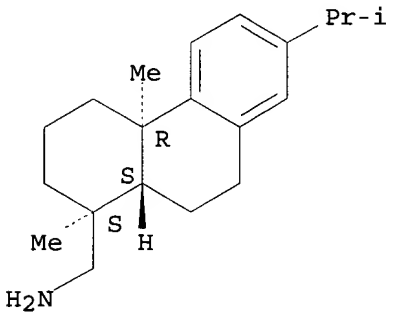
L2 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **77831-61-9** REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo-, (S)-, compd. with [1S-(1.alpha.,4a.beta.,10a.alpha.)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenemethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Phenanthrenemethanamine, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1.alpha.,4a.beta.,10a.alpha.)]-, (S)-6-oxo-2-piperidinecarboxylate (9CI)

FS STEREOSEARCH
MF C20 H31 N . C6 H9 N O3
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 77831-59-5
CMF C20 H31 N

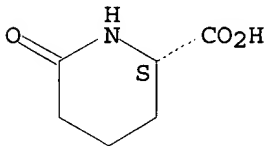
Absolute stereochemistry.



CM 2

CRN 34622-39-4
CMF C6 H9 N O3

Absolute stereochemistry.



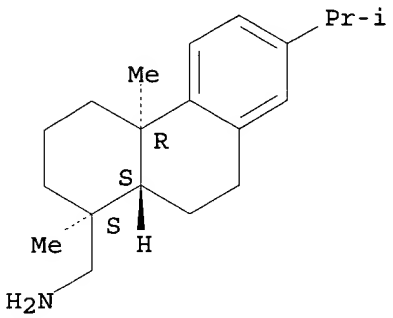
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **77831-60-8** REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo-, compd. with [1S-(1.alpha.,4a.beta.,10a.alpha.)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenemethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Phenanthrenemethanamine, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1.alpha.,4a.beta.,10a.alpha.)]-, (.+-.)-6-oxo-2-piperidinecarboxylate
CN 1-Phenanthrenemethanamine, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1.alpha.,4a.beta.,10a.alpha.)]-6-oxo-2-piperidinecarboxylate (9CI)
CN 2-Piperidinecarboxylic acid, 6-oxo-, (.+-.)-, compd. with [1S-(1.alpha.,4a.beta.,10a.alpha.)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenemethanamine (1:1)
FS STEREOSEARCH
MF C20 H31 N . C6 H9 N O3
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

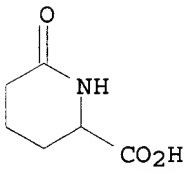
CRN 77831-59-5
CMF C20 H31 N

Absolute stereochemistry.



CM 2

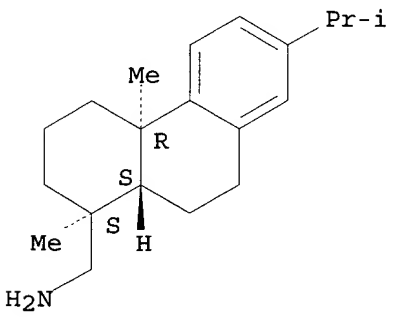
CRN 3770-22-7
CMF C6 H9 N O3



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **77831-59-5** REGISTRY
CN 1-Phenanthrenemethanamine, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1S-(1.alpha.,4a.beta.,10a.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H31 N
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, GMELIN*, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

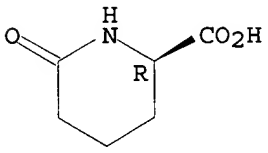


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **72002-30-3** REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo-, (R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN D-Pyrohomoglutamic acid
FS STEREOSEARCH
MF C6 H9 N O3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

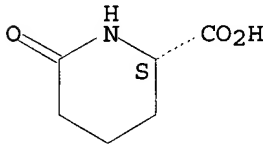


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **34622-39-4** REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Piperidinecarboxylic acid, 6-oxo-, (S)-
CN Pipecolic acid, 6-oxo-, L- (8CI)
OTHER NAMES:
CN (2S)-6-Oxopipecolic acid
CN 6-Oxo-L-pipecolic acid
CN L-Pyro-.alpha.-aminoadipic acid
CN L-Pyrohomoglutamic acid
FS STEREOSEARCH
MF C6 H9 N O3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

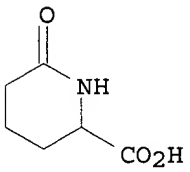
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

24 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
24 REFERENCES IN FILE CAPLUS (1967 TO DATE)

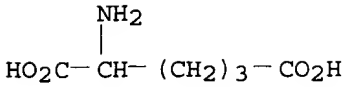
L2 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3770-22-7 REGISTRY
CN 2-Piperidinecarboxylic acid, 6-oxo- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pipecolic acid, 6-oxo- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 6-Oxo-2-piperidinecarboxylic acid
CN 6-Oxopipecolic acid
FS 3D CONCORD
DR **64520-52-1**
MF C6 H9 N O3
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

17 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L2 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 542-32-5 REGISTRY
CN Hexanedioic acid, 2-amino- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-2-Aminoadipic acid
CN .alpha.-Aminoadipic acid
CN 2-Aminoadipate
CN 2-Aminoadipic acid
CN DL-.alpha.-Aminoadipic acid
CN DL-2-Aminoadipic acid
CN DL-2-Aminohexanedioic acid
FS 3D CONCORD
DR **626-71-1, 82144-77-2**
MF C6 H11 N O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, NAPRALERT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

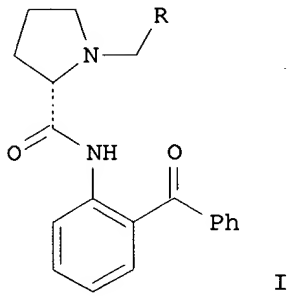
527 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
527 REFERENCES IN FILE CAPLUS (1967 TO DATE)
22 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

AN 1997:533615 CAPLUS
DN 127:205477
TI Preparation of **d**- or l-**threo-methylphenidate** by resolution and recycling of undesired enantiomers by epimerization.
IN Langston, Marianne; Zavareh, Hooshang Shahriari
PA Medeva Europe Ltd., UK
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9728124	A1	19970807	WO 1997-GB281	19970131
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2243534	AA	19970807	CA 1997-2243534	19970131
	AU 9716082	A1	19970822	AU 1997-16082	19970131
	AU 715183	B2	20000120		
	EP 879228	A1	19981125	EP 1997-902435	19970131
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000504008	T2	20000404	JP 1997-527425	19970131
PRAI	GB 1996-2174		19960202		
	GB 1996-18836		19960910		
	WO 1997-GB281		19970131		

AB Title process comprises resoln. of a mixt. of the enantiomers, **racemization** of the unwanted enantiomer to give a mixt. of all four stereoisomers, and sepn. of the erythro stereoisomers, to leave the threo mixt. of enantiomers for resoln. Thus, **d-threo-methylphenidate** was refluxed 4 h with propionic acid in PhMe to give a mixt. of all 4 stereoisomers. Resoln. is carried out using the method of PCT/GB97/00185.

AN 1997:633710 CAPLUS
DN 127:293572
TI Optimization of the retroracemization procedure for .alpha.-**amino acids** using (S)-2-[(N-alkylprolyl)amino]benzophenones, **recyclable** chiral auxiliaries
AU De, Binod B.; Thomas, Neil R.
CS Dep. Chem., Univ. Nottingham, University Part, Nottingham, NG7 2RD, UK
SO Tetrahedron: Asymmetry (1997), 8(16), 2687-2691
CODEN: TASYE3; ISSN: 0957-4166
PB Elsevier
DT Journal
LA English
OS CASREACT 127:293572
GI

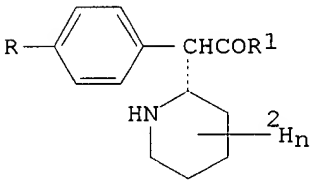


I

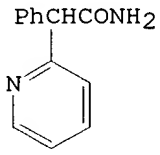
AB The retroracemization procedure developed by Y. N. Belokon, et al. (1992) has been re-examd. using a variety of new (S)-2-[(N-alkylprolyl)amino]benzophenones I (R = Ph, 1-naphthyl, 2-pyridyl, 3-pyridyl) as chiral auxiliaries. Benzophenones I (R = Ph, 1-naphthyl) in conjunction with Ni(NO3)2.cntdot.6H2O and a racemic .alpha.-amino acid preferentially form a single diastereoisomer in the presence of a mild base such as sodium methoxide. Decompn. of this complex under acidic conditions leads to the isolation of the (S)-amino acid in good yield, and in 55 to 99% e.e. The retroracemization abilities of I (R = polymer-bound Ph) have also been investigated and preliminary results for this are presented.

AN 83:114219 CA
TI Methyl **threo**-.alpha.-phenyl-.alpha.-(2-piperidyl)acetate hydrochloride
IN Yakhontov, L. N.; Levkoeva, E. I.
PA Ordzhonikidze, S., All-Union Scientific-Research Chemical-Pharmaceutical Institute, USSR
SO U.S.S.R.
From: Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki 1975, 52(13), 54.
CODEN: URXXAF
PI SU 466229 750405
AI SU 73-1874299 730123
DT Patent
LA Russian
AB The title phenylpiperidylacetate was prepd. by sapong. .alpha.-phenyl-.alpha.-(2-pyridyl)acetonitrile with aq.-alc. alkali, hydrogenating the resulting salt at 70.degree., 50-60 atm, and pH 7-9 over a Ni catalyst, isomerizing the resulting mixt. of **threo**- and erythro-phenylpiperidylacetate salts by heating in an alk. medium, acidifying to pH 6, and esterifying the resulting **threo**-.alpha.-phenyl-.alpha.-(2-piperidyl)acetic acid.

AN 97:144733 CA
TI Synthesis of deuterium-labeled methylphenidate, p-hydroxymethylphenidate, ritalinic acid, and p-hydroxyritalinic acid
AU Patrick, Kennerly; Kilts, Clinton; Breese, George
CS Biol. Sci. Res. Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SO J. Labelled Compd. Radiopharm. (1982), 19(4), 485-90
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
GI



I



VI

AB In the prepns. of the title compds. (I; R = H, OH, R1 = OMe; R = H, OH, R1 = OH) (II-V, resp.), all possible combinations of 2H on the piperidine ring were obtained, the most abundant being the pentadeuterated product. Deuteration of the amide VI gave a 70:30 erythro-**threo** mixt. I (R = H, R1 = NH2) which after KOH epimerization and treatment with HCl gave 74% IV.HCl. Subsequent esterification of IV.HCl gave 89% II.HCl. III.HCl and V.HBr were prepd. by modification of a previous method (1981). II-V were prepd. as internal stds. for mass fragmentog. assays of methylphenidate and its metabolites.

AN 55:48746 CA
OREF 55:9433e-f
TI Conversion of stereoisomers
IN Rometsch, Rudolf
PA Ciba Pharmaceutical Products, Inc.
DT Patent
LA Unavailable
FAN.CNT 1

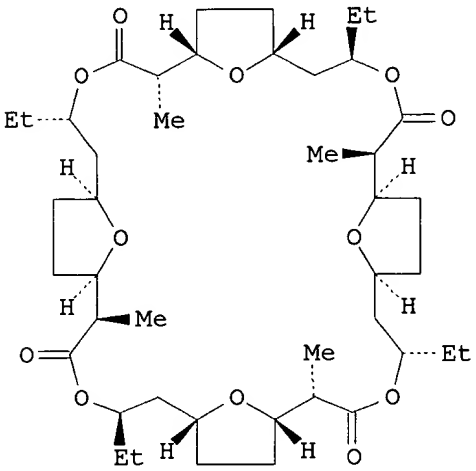
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2957880		19601025	US	<--

AB The a-racemates of .alpha.-aryl-.alpha.-(2-piperidyl)acetic acid and derivs. are converted to b-racemates by heating with alk. reagents at 100-20.degree.. The Me ester of b-antipode has a mild stimulating effect on the central nervous system while the Me ester of the a-form is almost inactive. Thus, to .alpha.-phenyl-.alpha.-(2-piperidyl)acetic acid Me ester-HCl 50 parts contg. 20% b-racemate in a little H2O and covered with an ether layer is added 1.5 equivs. aq. 50% KOH, the layers sepd., the H2O layer extd. with ether, the ether exts. evapd. to dryness, the residue mixed with KOH 50 and H2O 100 parts, the mixt. refluxed 4 hrs., cooled, the upper layer, contg. solid stereoisomeric acid racemates, dild. with H2O 110, and brought to pH 6 with 2N H2SO4 137 to ppt. b-racemate of .alpha.-phenyl-.alpha.-(2-piperidyl)acetic acid 24.2 parts.

AN 1967:411730 CAPLUS
DN 67:11730
TI Synthesis of .beta.-methyllanthionine
AU Belitz, Hans D.
CS Tech. Hochsch., Munich, Ger.
SO Tetrahedron Lett. (1967), (8), 749-51
CODEN: TELEAY
DT Journal
LA German
AB Synthetic .beta.-methyllanthionine (I), a component of the important bacterial peptide nisin, was obtained by refluxing DL-.beta.-methylcysteine (II) with H2C:C(NHAc)CO2H at pH 7.0 (N atm.) and subsequent hydrolysis of the N-Ac compd. II was produced from threonine according to Arnstein (CA 52: 12760f) and was assigned the **threo** configuration. Both .alpha.-C atoms were **racemized** and showed the presence of 3 components with relative areas 2:4:3 on chromatog. with Amberlite IR 120. A chromatogram of I with addn. of natural material from nisin showed a coincidental 2nd peak and for orientation of the components in a complete **amino acid** chromatogram that of a nisin hydrolyzate was used. I obtained synthetically from L-cysteine and CHMe:C(NHBz)CO2H (Schoeberl and Graefje, CA 56: 1519i) also showed the presence of 3 components of which the central peak behaved chromatographically as I prepd. from subtilin.

AN 1961:137502 CAPLUS
DN 55:137502
OREF 55:25949d-f
TI **Racemization** of LG(+)-**threo**-2,2-dimethyl-4-phenyl-5-amino-1,3-dioxane
AU Kamiya, Takashi
CS Fujisawa Pharm. Co., Osaka
SO Chem. & Ind. (London) (1961) 256
DT Journal
LA Unavailable
AB LG(+)**threo**-2,2-Dimethyl-4-phenyl-5-**amino**-1,3-dioxane (I), a hitherto useless intermediate obtained in the prepn. of chloramphenicol, was converted to the DG(-)-**threo**-isomer, a useful intermediate. LG(+)-**threo**-I treated with H2O2 in the presence of Na2WO4 at 10-15.degree. yielded 92% LG(-)-2,2-dimethyl-4-phenyl-5-hydroxyimino-1,3-dioxane (II), m. 141-2.degree. (.alpha.)D -78.4.degree., but no LG(-)-bis(2,2-dimethyl-4-phenyl-5-nitroso-1,3-dioxane (III). Refluxing LG(-)-II with excess NaOBu-tert in tert-BuOH gave 85% (.+-.)-II, m. 152-3.degree.. **Racemization** occurred only partially by use of primary and secondary alcs. and their aq. solns. (.+-.)-II reduced gave a mixt. of (.+-.)-**threo**- and **erythro**-I in 10:1 ratio (91% yield), which gave by subsequent resolution with D-dibenzoyltartaric **acid** and decompn. from its salts DG(-)-**threo**-I, b2 118-19.degree., [.alpha.]D -49.6.degree., in excellent yield.

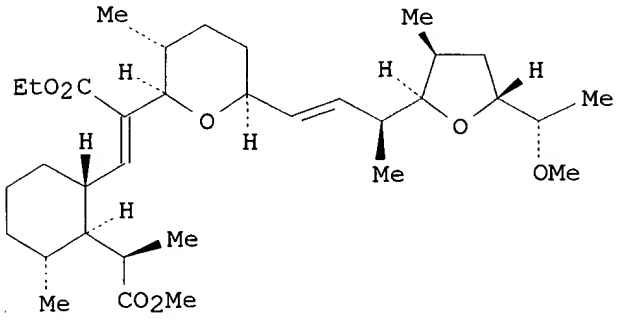
AN 1988:454529 CAPLUS
DN 109:54529
TI Synthesis of (+)- and (-)-homononactinic acid. Total synthesis of the macrotetrolide tetranactin by "Reverse Coupe du Roi". Structure correction for isodinactin
AU Schmidt, Ulrich; Werner, Juergen
CS Isotopenforsch., Univ. Stuttgart, Stuttgart, D-7000/80, Fed. Rep. Ger.
SO Synthesis (1986), (12), 986-92
CODEN: SYNTBF; ISSN: 0039-7881
DT Journal
LA German
OS CASREACT 109:54529
GI



I

AB The syntheses of (-)- and (+)-homononactic acid were achieved in 4 steps and 6 steps, resp., starting with the reaction of 2-lithio-5-vinylfuran with (S)-(-)-ethyloxirane. The vinyl group was transformed to the branched aldehyde by a regiospecific oxo reaction. Oxidn. to the carboxylic acid, esterification, and hydrogenation of the furan ring formed **four** diastereomers of Me homononactate. **Two** of these isomers were used directly for the synthesis of tetranactin (I), the others could be recycled by **epimerization** and sepn. The achiral I was constructed from **two** mols. of **chiral** (+)-homononactyl-(-)-homononactic acid by ester formation via the acid chloride and subsequent lactonization via the active thiocarboxylic S-(3-cyano-4,6-dimethyl-2-pyridinyl) ester. The structure of isodinactin was cor. to cyclo[(+)H-(-)H-(+)N-(-)N] (H = homononactyl, N-nonactyl) by comparing the optical rotations of Me nonactate and Me homononactate from natural origin with those of the optically pure synthetic compds.

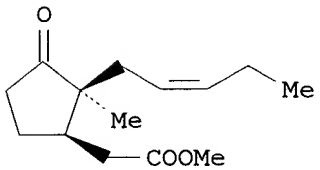
AN 1998:492163 CAPLUS
DN 129:244959
TI Synthesis of the acyltetronic acid ionophore tetronasin (ICI M139603)
AU Ley, Steven V.; Brown, Dearg S.; Clase, J. Andrew; Fairbanks, Antony J.; Lennon, Ian C.; Osborn, Helen M. I.; Stokes-Owen, Elaine S. E.; Wadsworth, David J.
CS Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK
SO J. Chem. Soc., Perkin Trans. 1 (1998), (15), 2259-2276
CODEN: JCPRB4; ISSN: 0300-922X
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 129:244959
GI



I

AB A synthetic strategy for the prepn. of tetronasin, an acyltetronic acid ionophore demonstrating antibiotic, antiparasitic and growth promotion in ruminants is described. The key step involves a metal mediated cyclization reaction which creates **two** rings and **four** new **stereocenters** in I in a highly efficient manner. The configurations of three of these **stereocenters** are as required for the synthesis of tetronasin. The remaining **stereocenter** is readily **epimerized** to the natural configuration at a later stage of the synthesis.

AN 1997:400248 CAPLUS
DN 127:147135
TI Importance of the chiral centers of jasmonic acid in the responses of plants
AU Holbrook, Larry; Tung, Pariana; Ward, Kerry; Reid, David M.; Abrams, Suzanne; Lamb, Nancy; Quail, J. Wilson; Moloney, Maurice M.
CS Department Biological Sciences, University Calgary, Calgary, AB, T2N 1N4, Can.
SO Plant Physiol. (1997), 114(2), 419-428
CODEN: PLPHAY; ISSN: 0032-0889
PB American Society of Plant Physiologists
DT Journal
LA English
GI



I

AB The importance of the **two chiral** centers at C-3 and C-7 in the mol. structure of jasmonic acid in plant responses was investigated. The authors sepd. Me jasmonate (MeJA) into (3R)- and (3S)-isomers with a fixed **stereochem.** at C-3, but **epimerization** at C-7 is possible. The **four** isomers of the nonepimerizable analog 7-Me MeJA were synthesized. These six esters and their corresponding acids were tested in three bioassays: (a) senescence in sunflower (Helianthus annuus) cotyledons; (b) proteinase inhibitor II gene expression in transgenic tobacco (Nicotiana tabacum) with .beta.-glucuronidase as a biochem. reporter; and (c) seed germination in Brassica napus and wheat (Triticum aestivum). The esters and acids had similar activities in the three assays, with the ester being more effective than its acid. The (3R)-**stereochem.** was crit. for jasmonate activity. Although activity was reduced after substituting the C-7 proton with a Me group, the analogs with (3R,7R)- or (3R,7S)-**stereochem.** were active in some of the assays. Although the **four** isomers of 7-Me MeJA were inactive or only weakly active in the senescence assay, they could overcome the senescence-promoting effect of (3R)-MeJA. The strongest antagonistic effect was obsd. with the (3R,7S)-isomer (I).

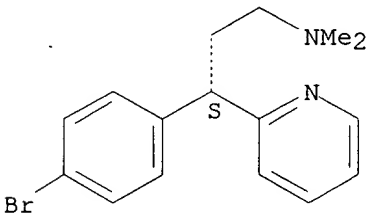
AN 1957:81299 CAPLUS
DN 51:81299
OREF 51:14640d-i,14641a-i,14642a-c
TI Studies in stereochemistry. XXVII. Conformational control of the migrating group in the deamination of 3-phenyl-2-butylamine
AU Cram, Donald J.; McCarty, John E.
CS Univ. of California, Los Angeles
SO J. Am. Chem. Soc. (1957), 79, 2866-75
DT Journal
LA Unavailable
AB D(-)-p-MeC6H4SO3CHMeCHMePh (4.92 g.), m. 64.8-5.1.degree., was converted by the method described previously to D(-)-MePh CHCH(NH2)Me (I), nD25 1.5157, .alpha.D25 -9.21.degree. (neat); the **enantiomer** of I (by direct **resolution**) had .alpha.D25 9.01.degree. (neat). The racemic acid phthalate of PhCH(OH)CHMe2 (II) **resolved** gave 24% active acid phthalate, m. 93.6-4.1,.degree. [.alpha.]D23 45.1.degree. (c 3.5, CHCl3), which hydrolyzed yielded 94% (+)-II, nD25 1.5113, [.alpha.]D23 48.3.degree. (c 6.7, Et2O). L(-)-**threo**-Isomer of MePhCHCH(OAc)Me (III), nD25 1.4877, .alpha.D25 -7.80.degree. (neat), was prepd. in 93% yield from L(+)-**threo** isomer of MePhCHCH(OH)Me (IV), nD25 1.5160, .alpha.D26 27.25.degree. (neat); similarly D(+)-**erythro**-III, nD25 1.4877, .alpha.D26 32.38.degree. (neat), in 96% from D(-)-**erythro**-IV, nD25 1.5168, .alpha.D25 -0.62.degree. (neat). (+)-II, nD25 1.5113, .alpha.D25 21.57.degree. (neat), gave 96% acetate (IVa), nD25 1.4853, .alpha.D26 104.68.degree. (neat). L(+)-I (4.63 g.), .alpha.D23 8.91.degree. (neat), nD25 1.5159, in 300 cc. dry glacial AcOH treated during 0.5 hr. with 31.4 g. KNO2 at 25-7.degree., the soln. stirred 1 hr. and shaken with 1.5 l. H2O and 200 cc. pure pentane, the aq. layer washed with pentane, and the combined pentane exts. washed, dried, and evapd., the residual oil dissolved in 100 g. glacial AcOH, the soln. kept 26 hrs. at 75.degree., cooled, dild. with 1 l. H2O, and extd. with pentane, the ext. washed, dried, and evapd., the residual oily mixt. of olefin, ketone, and acetates dissolved in 150 cc. MeOH contg. 15 cc. H2O, 15 g. Girard T reagent, 4.1 g. NaOAc, and 3.0 g. glacial AcOH, the soln. refluxed 1.5 hrs., cooled, dild. with 1 l. H2O, and extd. with pentane, the pentane ext. washed, dried, and evapd., the residual oil dissolved in dry Et2O and added with stirring to 1.3 g. LiAlH4 in Et2O, the excess LiAlH4 decompd. with dil. HCl, the aq. layer extd. with pentane, the combined Et2O and pentane solns. washed, dried, and evapd., the residual oil chromatographed on 150 g. Al2O3 from pentane, and the column washed with pentane gave 0.43 g. olefin fraction; further elution with EtOH yielded 1.86 g. mixt. of diastereomeric IV and II, .alpha.D23 3.18.degree. (neat), nD25 1.5167; 0.74 g. of the mixt. treated with pyridine-Ac2O yielded 95% acetate, .alpha.D24 -27.55.degree. (neat), nD25 1.4874; 0.90 g. of the alc. fraction treated 18 hrs. at 75.degree. with 25 cc. glacial AcOH contg. 2.5 g. Ac2O and 0.25 g. p-MeC6H4SO3H.H2O (this treatment completely **racemizes** and partly converts the II to olefin and leaves the diastereomeric IV intact), the mixt. cooled, dild. with 400 cc. H2O, and extd. with pentane, the pentane ext. washed, dried, and evapd., the residual oil dissolved in dry Et2O and added to 0.3 g. LiAlH4, the resulting olefin-alc. mixt. isolated in the usual way and chromatographed on 50 g. Al2O3, and the fraction eluted with MeOH and distd. at 15 mm. yielded 0.72 g. oil, .alpha.D23 3.21.degree. (neat); a sample (0.43 g.) treated with Ac2O-pyridine yielded 95% acetate,

.alpha.D26 -26.96.degree. (neat), nD25 1.4879. Similar deamination of 4.70 g. D(-)-**threo**-I, .alpha.D23 -42.33.degree. (neat), nD26 1.5143, gave 0.53 g. olefin and 1.80 g. mixt. of the 3 isomeric alcs., .alpha.D23 -5.78 (neat), nD25 1.5143; infrared analysis of the alc. indicated the presence of 36 (35) % **threo**-IV, 33 (33) % **erythro**-IV, and 30 (32) % II; a sample of the alc. mixt. treated with pyridine-Ac2O yielded 96% acetate, .alpha.D23 0.05.degree. (neat), nD25 1.4869; a sample (0.86 g.) of the alc. mixt. treated with p-MeC6H4SO3H in AcOH gave 0.61 g. mixt. or 2 active diastereomers and d-II, .alpha.D23 -4.21.degree. (neat), which treated with Ac2O-pyridine yielded 94% acetate, .alpha.D26 8.41.degree. (neat), nD25 1.4872. L(+)-**threo**-I (9.83 g.), .alpha.D24 6.42.degree. (neat), nD25 1.5142, acetolyzed in the usual manner, the resulting mixt. treated directly with Girard T reagent, and the product reduced with LiAlH4 and chromatographed on Al2O3 yielded 1.03 g. olefin fraction and 4.90 g. alc. fraction. Olefin fraction (0.51 g.) in 25 cc. MeOH hydrogenated over Pt black (from 50 mg. PtO2), the mixt. filtered, the filtrate shaken with 350 cc. H2O and pentane, the pentane layer washed, dried, and evapd., the residual oil distd., and the crude distillate (0.45 g.) carefully fractionated gave 0.23 g. L(+)-EtMeCHPh, .alpha.D23 3.82.degree. (neat), nD25 1.4878 (15.8% optically pure) (thus only optically pure MePhCHCH:CH2 (V) survived the deaminative solvolysis). Alc. fraction (2.00 g.) treated with AcOH, Ac2O, and p-MeC6H4SO3H, and the product reduced with LiAlH4 and chromatographed in the usual manner gave 0.38 g. olefin, nD25 1.5190, and 1.09 g. alc. fraction, .alpha.D23 0.63.degree. (neat), nD25 1.5147, which analyzed by infrared spectroscopy showed the presence of 33 (34) % **threo**-IV, (25) % **erythro**-IV, and 42 (42) % II; it gave with Ac2O-pyridine 96% acetate, .alpha.D24 -1.18.degree. (neat), nD25 1.4873. D(-)-I (10.0 g.), .alpha.D25 -4.01 (neat), nD25 1.5160, gave similarly 0.463 g. olefin and 5.05 g. alc.; the olefin fraction reduced yielded 0.396 g. D(-)-EtMeCHPh, nD25 1.4878, .alpha.D24 -8.70.degree. (neat) (26% optically pure); 2.00 g. of the alc. fraction treated with p-MeC6H4SO3H, reduced with LiAlH4, and chromatographed yielded 0.215 g. olefin and 1.22 g. alc. fraction, nD26 1.5166, .alpha.D24 -1.42.degree. (neat), which subjected to infrared analysis showed the presence of 8 (9) % **threo**-IV, 84 (84) % **erythro**-IV, and 9 (8) % II; it gave with Ac2O-pyridine 94% acetate, .alpha.D24 12.53.degree. (neat). (-)-**threo**-I (35% optically pure) subjected to a deaminative solvolysis in the usual manner, a portion (0.78 g.) of the alc. product (not treated with p-MeC6H4SO3H) converted to its acid phthalate, the resulting oil subjected to a partition chromatography on 164 g. 1:2 SiO2-Celite (made up with 1% EtOH in CHCl3), the column eluted with 1% EtOH in CHCl3, and the resulting cryst. material recrystd. from CHCl3-pentane yielded 9 mg. acid phthalate of dl-II, m. 131.8-2.2.degree.. (+)-II (7.0 g.), .alpha.D26 21.57.degree. (neat), nD25 1.5113, heated 3 hrs. on the steam bath with 30.0 g. Ac2O and 75 g. pyridine, dild. with 250 cc. H2O and 100 g. ice, and extd. with pentane, the ext. washed, dried, and evapd., and the residual oil chromatographed on 140 g. Al2O3 gave 8.5 g. (+)-IVa, .alpha.D26 104.68.degree. (neat), nD25 1.4853. L(-)-**threo**-III (0.89 g.), .alpha.D24 -7.80.degree. (neat), nD25 1.4877, and 0.90 g. (+)-IVa,

.alpha.D26 104.68.degree. (neat), nD25 1.4853, mixed, the mixt., .alpha.D25 41.72.degree. (neat), nD25 1.4870, treated with 0.60 g. MePhC(OAc)Et (VI), nD25 1.4946, 0.20 g. AcPh, nD25 1.5343, and 0.09 g. AcCHMePh, nD25 1.5104, subjected to the exact conditions of the deamination reaction and processed in the usual manner yielded 0.38 g. olefin, nD25 1.5214, and 1.00 g. alc. fraction; a sample of the alc. (0.60 g.) gave with Ac2O-pyridine 0.65 g. acetate, nD25 1.4871, .alpha.D24 41.84 (neat). (+)-PhCH(OAc)CHMe2 (VII) (1.03 g.), .alpha.D26 104.7.degree. (neat), was prepd. from (+)-II, .alpha.D26 21.57.degree. (neat), nD25 1.5113; the VII reduced in the usual manner with LiAlH4 gave 0.83 g. (+)-II, nD25 1.5112, .alpha.D26 21.59.degree. (neat). (+)-VII (1.00 g.), .alpha.D26 104.7.degree. (heat), nD25 1.4853, 20 cc. glacial AcOH, and 0.8 cc. Ac2O heated 26 hrs. at 75.degree. gave 0.96 g. unchanged (+)-VII, .alpha.D26 104.3.degree. (neat), nD25 1.4853. D(-)-V (0.28 g.), .alpha.D23 -5.62.degree. (neat), nD25 1.5054, 0.13 g. cis-MePhC:CHMe (VIII), nD25 1.5402, and 0.08 g. trans-VIII, nD25 1.5193, in 100 cc. glacial AcOH treated during 0.5 hr. with stirring with 10.3 g. solid KNO2 in 8 portions, the mixt. stirred 45 min., the product isolated by the general procedure (treatment with Girard T reagent was omitted), and the olefin fraction hydrogenated in 25 cc. MeOH at 22.degree. and 750 ram. over 25 mg. PtO2 yielded 0.15 g. (-)-MeEtCHPh, nD25 1.4878, .alpha.D24 -23.62.degree. (neat). EtMeC(OH)Ph (1.00 g.), nd25 1.5167, and 0.90 g. (+)-II, .alpha.D24 21.34.degree. (neat), nD25 1.5113, heated 18 hrs. at 75.degree. with 25 cc. glacial AcOH contg. 2.5 g. Ac2O and 0.25 g. p-MeC6H4SO3H.H2O, and the product isolated, reduced with LiAlH4 and chromatographed in the usual manner gave 0.89 g. olefin, nD25 1.5192, and 0.61 g. recovered (+)-II, nD25 1.5113, .alpha.D24 0.13.degree. (neat) (corresponding to 99.4% **racemization**). L(+)-IV (0.90 g.), .alpha.D25 31.61.degree., nD25 1.5166, 25 g. glacial AcOH, 2.5 g. Ac2O, and 0.25 g. p-MeC6H4SO3H.H2O kept 18 hrs. at 75.degree. gave similarly 0.72 g. L(+)-IV, .alpha.D24 31.51.degree. (neat), nD25 1.5164, but no olefin. (+)-II (0.010 g.), .alpha.D23 21.21.degree. (neat), nD25 1.5113, 0.082 g. dl-II, nD25 1.5113, 0.103 g. L(+)-**threo**-IV, .alpha.D25 31.61.degree. (neat), nD25 1.5167, and 0.917 g. L(+)-**erythro**-IV, .alpha.D26 0.76.degree. (neat), nD25 1.5163, mixed, and a portion of the mixt. (1), .alpha.D24 4.52.degree. (neat), nD25 1.5167, treated with Ac2O-pyridine yielded 93% acetate, .alpha.D24 0.50.degree.-25.9.degree. (neat). (+)-II (0.068 g.), 0.356 g. dl-II, 0.108 g. L(+)-**threo**-IV, 0.199 g. L(+)-**erythro**-IV, 0.215 g. dl-**threo**-IV, nD25 1.5167, and 0.063 g. dl-**erythro**-IV, nD25 1.5163, mixed, and a portion of the mixt. (2) treated with Ac2O-pyridine gave 92% acetate, .alpha.D24 -0.50.degree. (neat). Mixts. 1 and 2 (0.50 g. each) treated 18 hrs. at 75.degree. with AcOH and p-MeC6H4SO3H and the product reduced with LiAlH4 and chromatographed in the usual manner yielded 0.36 g. alc., .alpha.D24 4.59.degree. (neat) (acetate, 92% yield, .alpha.D26 -28.49.degree.), from mixt. 1, and 0.30 g. alc., .alpha.D24 4.75.degree. (acetate, .alpha.D26 -8.72.degree.), from mixt. 2. (+)-II (0.529 g.), .alpha.D22 20.41.degree. (neat), and 250 cc. 0.32N NaOH brought to reflux and steam-distd. and the product isolated in the usual way gave 0.465 g. unchanged (+)-II, .alpha.D23 20.60.degree. (neat).

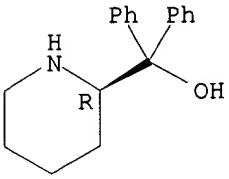
AN 70:96027 CA
TI Absolute configurations of the pheniramines, methyl phenidates, and pipradrols
AU Shafi'ee, Abbas; Hite, Gilbert
CS Coll. of Pharm. Sci., Columbia Univ., New York, N. Y., USA
SO J. Med. Chem. (1969), 12(2), 266-70
CODEN: JMCMAR
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Abs. configurations of the 16 optical isomers of seven structurally related title compds. of biol. interest were detd. The pheniramines were converted to a Me **phenidate** in which the relative configurations of the two asymmetric centers were established. The endocyclic center of asymmetry introduced in the process was maintained intact while the asymmetry of the exocyclic center was destroyed in the conversion to a pipradrol deriv. This was related to pipradrol by an aufbau sequence starting with (R)-(+)-piperidine-2-carboxylic acid. The absolute configurations of deoxypipradrol and thiopipradrol were established by Birch redn. and by rotatory dispersion, resp. The antihistaminically more active acid maleates of Ia and Ib are stereochemically superimposable upon Ic and all have the (S)-configuration. The analeptically more active hydrochlorides of **threo**-Me **phenidate**, pipradol, and thiopipradrol are stereochemically superimposable upon II. These have the (2R:2'R), (R), (S), and (R) configurations, resp., but are not stereochem. superimposable upon the analeptically more active (+) acid sulfate of amphetamine.
IT **132-21-8 301-24-6 18652-12-5**
19141-45-8 19141-46-9 23201-92-5
23201-94-7 23202-01-9 23202-02-0
RL: PRP (Properties)
(abs. configuration of)
RN 132-21-8 CA
CN 2-Pyridinepropanamine, .gamma.-(4-bromophenyl)-N,N-dimethyl-, (.gamma.S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 301-24-6 CA
RN 18652-12-5 CA
CN 2-Piperidinemethanol, .alpha.,.alpha.-diphenyl-, hydrochloride, (R)-(9CI)
(CA INDEX NAME)

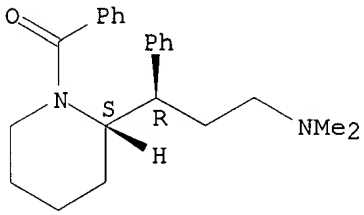
Absolute stereochemistry.



● HCl

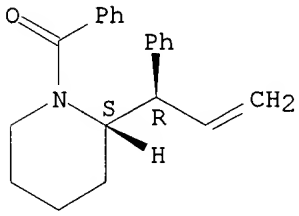
RN 19141-45-8 CA
CN Piperidine, 1-benzoyl-2-[.alpha.-[2-(dimethylamino)ethyl]benzyl]-, erythro-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



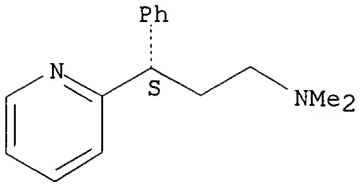
RN 19141-46-9 CA
CN Piperidine, 1-benzoyl-2-(1-phenylallyl)-, erythro-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



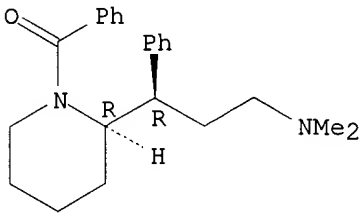
RN 23201-92-5 CA
CN 2-Pyridinepropanamine, N,N-dimethyl-.gamma.-phenyl-, (.gamma.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



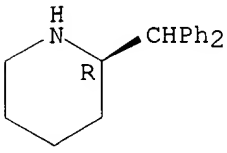
RN 23201-94-7 CA
CN Piperidine, 1-benzoyl-2-[.alpha.-[2-(dimethylamino)ethyl]benzyl]-, threo-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RN 23202-01-9 CA
CN Piperidine, 2-(diphenylmethyl)-, hydrochloride, (R)- (9CI) (CA INDEX NAME)

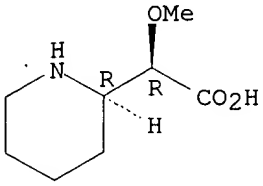
Absolute stereochemistry.



● HCl

RN 23202-02-0 CA
CN 2-Piperidineacetic acid, .alpha.-methoxy-, hydrochloride, (.alpha.R,2R)- (8CI) (CA INDEX NAME)

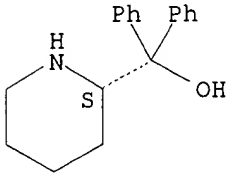
Absolute stereochemistry.



● HCl

IT **18720-89-3P 19141-47-0P 19141-48-1P**
19141-49-2P 19141-50-5P 19210-22-1P
19210-23-2P 19210-24-3P 20306-87-0P
23201-96-9P 23201-98-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 18720-89-3 CA
CN 2-Piperidinemethanol, .alpha.,.alpha.-diphenyl-, hydrochloride, (S)-(8CI)
(CA INDEX NAME)

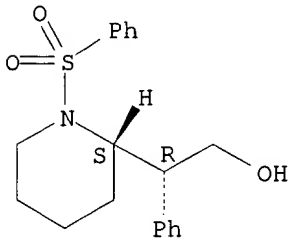
Absolute stereochemistry.



● HCl

RN 19141-47-0 CA
CN 2-Piperidineethanol, .beta.-phenyl-1-(phenylsulfonyl)-, erythro-(-)-(8CI)
(CA INDEX NAME)

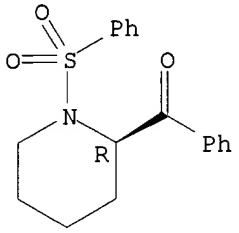
Rotation (-). Absolute stereochemistry unknown.



RN 19141-48-1 CA

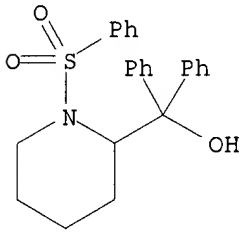
CN Piperidine, 2-benzoyl-1-(phenylsulfonyl)-, (R)-(-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



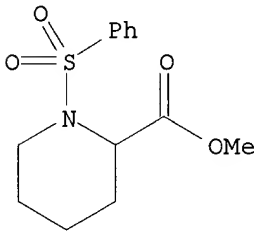
RN 19141-49-2 CA
CN 2-Piperidinemethanol, .alpha.,.alpha.-diphenyl-1-(phenylsulfonyl)-, (-)- (8CI) (CA INDEX NAME)

Rotation (-).



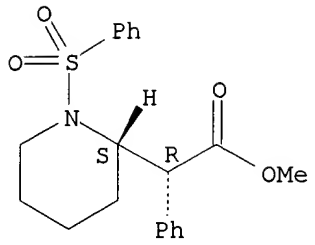
RN 19141-50-5 CA
CN Pipecolic acid, 1-(phenylsulfonyl)-, methyl ester, (+)- (8CI) (CA INDEX NAME)

Rotation (+).



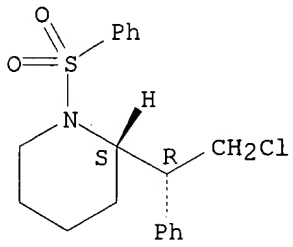
RN 19210-22-1 CA
CN 2-Piperidineacetic acid, .alpha.-phenyl-1-(phenylsulfonyl)-, methyl ester, erythro-(-)- (8CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.

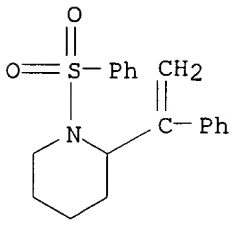


RN 19210-23-2 CA
CN Piperidine, 2-[.alpha.-(chloromethyl)benzyl]-1-(phenylsulfonyl)-, erythro-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

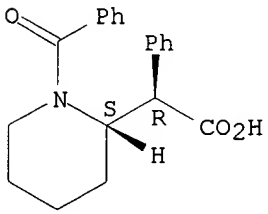


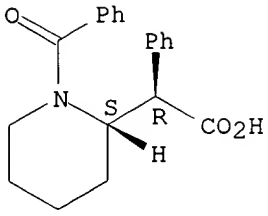
RN 19210-24-3 CA
CN Piperidine, 1-(phenylsulfonyl)-2-(1-phenylvinyl)-, stereoisomer (8CI) (CA
INDEX NAME)



RN 20306-87-0 CA
CN 2-Piperidineacetic acid, 1-benzoyl-.alpha.-phenyl-, erythro-(-)- (8CI) (CA INDEX NAME)

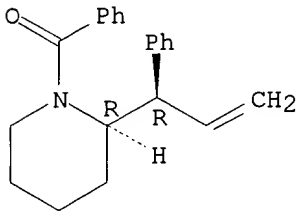
Rotation (-). Absolute stereochemistry unknown.





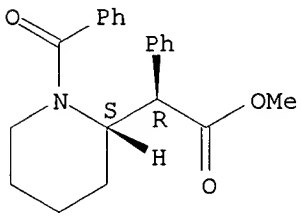
RN 23201-96-9 CA
CN Piperidine, 1-benzoyl-2-(1-phenylallyl)-, threo-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RN 23201-98-1 CA
CN 2-Piperidineacetic acid, 1-benzoyl-.alpha.-phenyl-, methyl ester, (R*,S*)-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.



AN 1993:496123 CAPLUS
DN 119:96123
TI Partial synthesis of five new analogs of the peptido-lactone virginiamycin S1, modified in the fifth and/or sixth position ([Xxx5]-VS1 with Xxx = Ala, Asp, Asn and Lys and [Ala5,Gly6]-VS1)
AU Moerman, Marc C.; Anteunis, Marc J. O.
CS Lab. Org. Chem., State Univ. Ghent, Ghent, Belg.
SO Int. J. Pept. Protein Res. (1993), 41(2), 102-17
CODEN: IJPPC3; ISSN: 0367-8377
DT Journal
LA English
OS CASREACT 119:96123
GI For diagram(s), see printed CA Issue.
AB Title virginiamycin S1 (VS1) analogs I (Abu = 2-aminobutyric acid) and II (Phg = 2-phenylglycine; Xxx = Ala, Lys, Asp, Asn) were prepd. from VS1-pentapeptide III, which was obtained by a **two**-step degrdn. process of the native antibiotic VS1. The MePhe residue was **epimerized** during the synthesis and the DL-Phg residue was used; therefore, I was obtained as 2 **epimers** due to the D and L centers at the MePhe residue and II were obtained as 4 diastereoisomers due to the D and L centers at the MePhe and Phg residues. Protecting groups during the procedure were chosen in order to realize a minimal no. of steps. Most of these gave excellent yields, including final cyclization between the fourth and fifth residue. II (Xxx = Lys) (trifluoroacetic acid salt) is water-sol., which is an important characteristic for eventual application of VS1 as a pharmaceutical agent. After cyclization a total of **four epimers** that have been sepd. by preparative TLC. The **chiral** identity of the final residues was realized by GC (Chirasil Val.RTM.-III) on the total hydrolyzates.

AN 1956:4517 CAPLUS
DN 50:4517
OREF 50:866c-i,867a-d
TI Chloramphenicol. IX. The racemization of substituted .alpha.-acylamino-.beta.-hydroxypropiophenones
AU Alberti, Carlo G.; Bernardi, Luigi; Camerino, Bruno; Cattapan, Domenico; Larini, Giovanni; Vercellone, Alberto
CS Lab. sci. e ricerche soc. anon. Farmaceutici Italia, Milan
SO Gazz. chim. ital. (1954), 84, 512-18
DT Journal
LA Unavailable
AB The transformation of .alpha.-acylamino-.beta.-acyloxypropiophenones by alk. catalysts into .alpha.-acylaminoacrylophenones is investigated. The .beta.-hydroxypropiophenones are prepd. by N-acylation of the HCl salts of the .alpha.-**amino**-.beta.-hydroxypropiophenones obtained by **acid** sapon. of the corresponding .alpha.-acylamino-.beta.-acyloxypropiophenones by the method of Scoffone and Iliceto (C.A. 47, 4303c). Thus, aq. D-**threo**-1-phenyl-1,3-diacetoxy-2-aminopropan-1-ol-HCl (10.5 g. in 21 cc.) and 3.6 g. NaHCO3 in 30 cc. H2O kept ice-cold overnight, and the ppt. recrystd. from water give 10 g. D-**threo**-1-phenyl-2-acetamino-3-acetoxy-propan-1-ol (I), m. 121-2.degree., [.alpha.]D -6.7 .+-. 1.degree. (c 4.0, MeOH). K2Cr2O7 (13 g. in 56 cc. H2O, 9.5 cc. AcOH, and 17 cc. concd. H2SO4) added dropwise to 11 g. I in 69 cc. CHCl3 and 12 cc. glacial AcOH at 5-10.degree., let stand at room temp., the CHCl3 layer washed with aq. NaHSO3, dil. H2SO4, aq. Na2CO3, and H2O and evapd., and the product recrystd. from EtOH gives 5.5 g. L-.alpha.-acetamino-.beta.-acetoxypropiophenone (II), m. 106-7.5.degree., [.alpha.]D 37.5 .+-. 1.degree. (c 4.0, MeOH). II (5.1 g.), 8 cc. concd. HCl, and 6.4 cc. H2O heated to complete soln., evapd. in vacuo, and the oil treated with MeOH and carboraffin give 1.8 g. L-.alpha.-amino-.beta.-hydroxypropiophenone-HCl (III), m. 179-80.degree. (decompn.), [.alpha.]D 42.5 .+-. 0.5.degree. (c 2.0, MeOH). The alc. liquor yields 1 g. more. BzCl (6.5 cc.) mixed with 10.5 g. NaOAc in 15 cc. H2O and added dropwise to 8 g. III in ice water at 0-5.degree., let stand 3 hrs. at room temp., and the ppt. washed gives 9 g. L-.alpha.-benzamino-.beta.-hydroxypropiophenone (IV), m. 138-40.degree. (from EtOH), [.alpha.]D -32.5 .+-. 1.5.degree. (c 2.0, MeOH). The D-p-nitro-.alpha.-acylamino-.beta.-hydroxypropiophenones were prepd. by N-acylation of the corresponding D-p-nitro-.alpha.-amino-.beta.-hydroxypropiophenone-HCl. Thus, 14 g. D-p-nitro-.alpha.-acetamino-.beta.-acetoxypropiophenone and 15 cc. concd. HCl heated 20 min. on a steam bath, filtered hot with carboraffin, made ice-cold, and the ppt. recrystd. from boiling 90% EtOH give 55% D-p-nitro-.alpha.-amino-.beta.-hydroxypropiophenone-HCl (V), m. 192-3.degree., [.alpha.]D -55 .+-. 1.5.degree. (c 4.0, 3% HCl). Aq. NaOAc (22 g. in 30 cc.) added slowly to 17 g. V, 50 cc. H2O, 100 g. ice, and 8 cc. Ac2O, agitated overnight, and the ppt. purified by 90% EtOH gives 11 g. D-p-nitro-.alpha.-acetamino-.beta.-hydroxypropiophenone (VI), yellowish, m. 145-6.degree., [.alpha.]D -21 .+-. 1.degree. (c 2.0, EtOH). The following .beta.-hydroxypropiophenones in addn. to VI were prepd.: L-.alpha.-benzamino (VII), m. 138-40.degree., [.alpha.]D -32.5 .+-. 1.5.degree. (c 2.0, MeOH); DL-.alpha.-benzamino (VIII), m. 141-2.degree. (cf. Long and Troutman, C.A. 44, 568f); DL-p-nitro-.alpha.-acetamino, m.

166-7.degree. (cf. L. and T., C.A. 44, 568i); D-p-nitro-.alpha.-benzamino (IX), m. 149-51.degree., [.alpha.]D 60 .+-. 1.degree. (c 2.0, Me2CO); DL-p-nitro-.alpha.-benzamino, m. 158-9.degree. (cf. S. and I., loc. cit.); D-p-nitro-.alpha.-propionamino (X), m. 134-5.degree., [.alpha.]D -26.5 .+-. 1.degree. (c 4.0, EtOH); DL-p-nitro-.alpha.-propionamino, m. 113-15.degree. (cf. S. and I., loc. cit.); D-p-nitro-.alpha.-chloroacetamino, m. 100-1.degree., [.alpha.]D 6.4 .+-. 1.degree. (c 2.0, EtOH); DL-p-nitro-.alpha.-chloroacetamino, m. 130-1.degree. (cf. S. and I., loc. cit.). The **racemization** of these compds. is exemplified by the following syntheses: VII (1 g.) in 10 cc. C5H5N and 10 cc. NEt3, let stand 3 hrs., poured into ice-HCl, and the product purified by EtOH, give 0.82 g. DL-.alpha.-benzamino-.beta.-hydroxypropiophenone, m. 141-2.degree. (cf. L. and T., loc. cit.). VI (20 g.) in 50 cc. C5H5N (dark red soln.) poured into 200 g. ice and 100 cc. concd. HCl and let stand ppts. 17.2 g. DL-p-nitro-.alpha.-acetamino-.beta.-hydroxypropiophenone (XII), m. 163-4.degree. (cf. L. and T., loc. cit.). A suspension of 20 g. VI in 100 cc. EtOH and 1 g. C5H5N, agitated 90 min., yield 17 g. XII. If, instead, the mixt. is refluxed 1 hr., 12 g. p-nitro-.alpha.-acetaminoacrylophenone, m. 121-2.degree. (cf. A., et al., C.A. 49, 8247d), is obtained. A suspension of 10 g. VI in 100 cc. HNEt2 agitated 10 min. gives 8.8 g. XII. VI (10 g.) in 100 cc. C5H5N let stand 3 days, poured into 300 g. ice and 200 cc. concd. HCl, and let stand gives 7.5 g. XII. A suspension of VI in NEt3 or 1-ethylpiperidine, agitated 4 hrs., and poured into ice-HCl, gives 85% XII. The velocity consts. of the 1st order are detd. by the decrease of rotatory power of 10% C5H5N solns. For the following propiophenones the K values (in hr.-1 .times. 102) and the acid dissocn. consts. (.times. 105) of the acylant acid, resp., are given: VI, 1.1 .+-. 0.15, 1.82; X, 1.2 .+-. 0.15, 1.34; VIII, 3.1 .+-. 0.1, 6.27; VII, 0, 6.27. These values show the strong influence of the p-NO2 group and the close relation between the energy of the acylant acid, NH2 group, and velocity of **racemization**. The K value of XI could not be detd. precisely because of the strong color, but the indications were that it was the highest value of all. The **racemization** of the propiophenones is of importance because of the possibility of utilizing the L-**threo** and D-**erythro** derivs. of phenylaminopropanediol, which heretofore have been waste products in the synthesis of chloroamphenicol. A mechanism is proposed and discussed.

AN 1977:30071 CAPLUS
DN 86:30071
TI L-(-)-2-Amino-3-(3,4-dihydroxyphenyl)propionic acid
IN Halmos, Jozsef; Meszaros, Robert; Jeszenszki, Andor
PA E. Gy. T. Gyogyszervegyeszeti Gyar, Hung.
SO Hung. Teljes, 22 pp.
CODEN: HUXXBU
DT Patent
LA Hungarian
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	HU 12041	O	19760828	HU 1971-EE1918	19710518
	HU 173178	P	19790328		

AB L-dopa (I) was prepd. by treating vanillin or piperonal (II) with glycine and Ac2O in the presence of Et3N, hydrolyzing the oxazolone intermediate at pH 4-11, hydrogenating, **resolving** with L-(+)-**threo**-1-(p-nitrophenyl)-2-amino-1,3-propanediol (III), and hydrolyzing with acid. The D-**enantiomer** was **racemized** with Ac2O and recirculated. Thus, a mixt. of II 170, glycine 102, and Ac2O 545 kg was treated with 164 kg Et3N, heated for 40 hr at 90.degree., and filtered at O.degree.. The product was stirred with aq. Na2CO3 at 90-100.degree. until homogeneous. Raney Ni was added and the mixt. was hydrogenated, filtered, acidified with HCl to pH 1.3, and filtered. A mixt. of the product, 150 kg recirculated **racemized** .alpha.-acetylamino-.beta.-(3,4-methylenedioxyphenyl)propionic acid, EtOH, and 200 kg III was heated to 50-60.degree., filtered, and cooled. The product was dissolved in 600 l. H2O and acidified with HCl to pH 1.3 at 0-5.degree.. A mixt. of the product, HCl 200, H2O 30, and PhOH 160 kg was heated for 22 hr at 105-8.degree. to give 33.9% I (based on II) in 99% purity.

the .alpha.-**amino**-.beta.-hydroxypropiophenones obtained by **acid** sapon. of the corresponding .alpha.-acylamino-.beta.-acyloxypropiophenones by the method of Scoffone and Iliceto (C.A. 47, 4303c). Thus, aq. D-**threo**-1-phenyl-1,3-diacetoxy-2-aminopropan-1-ol-HCl (10.5 g. in 21 cc.) and 3.6 g. NaHCO3 in 30 cc. H2O kept ice-cold overnight, and the ppt. recrystd. from water give 10 g. D-**threo**-1-phenyl-2-acetamino-3-acetoxy-propan-1-ol (I), m. 121-2.degree., [.alpha.]D -6.7 .+-. 1.degree. (c 4.0, MeOH). K2Cr2O7 (13 g. in 56 cc. H2O, 9.5 cc. AcOH, and 17 cc. concd. H2SO4) added dropwise to 11 g. I in 69 cc. CHCl3 and 12 cc. glacial AcOH at 5-10.degree., let stand at room temp., the CHCl3 layer washed with aq. NaHSO3, dil. H2SO4, aq. Na2CO3, and H2O and evapd., and the product recrystd. from EtOH gives 5.5 g. L-.alpha.-acetamino-.beta.-acetoxypropiophenone (II), m. 106-7.5.degree., [.alpha.]D 37.5 .+-. 1.degree. (c 4.0, MeOH). II (5.1 g.), 8 cc. concd. HCl, and 6.4 cc. H2O heated to complete soln., evapd. in vacuo, and the oil treated with MeOH and carboraffin give 1.8 g. L-.alpha.-**amino**-.beta.-hydroxypropiophenone-HCl (III), m. 179-80.degree. (decompn.), [.alpha.]D 42.5 .+-. 0.5.degree. (c 2.0, MeOH). The alc. liquor yields 1 g. more. BzCl (6.5 cc.) mixed with 10.5 g. NaOAc in 15 cc. H2O and added dropwise to 8 g. III in ice water at 0-5.degree., let stand 3 hrs. at room temp., and the ppt. washed gives 9 g. L-.alpha.-benzamino-.beta.-hydroxypropiophenone (IV), m. 138-40.degree. (from EtOH), [.alpha.]D -32.5 .+-. 1.5.degree. (c 2.0, MeOH). The D-p-nitro-.alpha.-acylamino-.beta.-hydroxypropiophenones were prepd. by N-acylation of the corresponding D-p-nitro-.alpha.-**amino**-.beta.-hydroxypropiophenone-HCl. Thus, 14 g. D-p-nitro-.alpha.-acetamino-.beta.-acetoxypropiophenone and 15 cc. concd. HCl heated 20 min. on a steam bath, filtered hot with carboraffin, made ice-cold, and the ppt. recrystd. from boiling 90% EtOH give 55% D-p-nitro-.alpha.-**amino**-.beta.-hydroxypropiophenone-HCl (V), m. 192-3.degree., [.alpha.]D -55 .+-. 1.5.degree. (c 4.0, 3% HCl). Aq. NaOAc (22 g. in 30 cc.) added slowly to 17 g. V, 50 cc. H2O, 100 g. ice, and 8 cc. Ac2O, agitated overnight, and the ppt. purified by 90% EtOH gives 11 g. D-p-nitro-.alpha.-acetamino-.beta.-hydroxypropiophenone (VI), yellowish, m. 145-6.degree., [.alpha.]D -21 .+-. 1.degree. (c 2.0, EtOH). The following .beta.-hydroxypropiophenones in addn. to VI were prepd.: L-.alpha.-benzamino (VII), m. 138-40.degree., [.alpha.]D -32.5 .+-. 1.5.degree. (c 2.0, MeOH); DL-.alpha.-benzamino (VIII), m. 141-2.degree. (cf. Long and Troutman, C.A. 44, 568f); DL-p-nitro-.alpha.-acetamino, m. 166-7.degree. (cf. L. and T., C.A. 44, 568i); D-p-nitro-.alpha.-benzamino (IX), m. 149-51.degree., [.alpha.]D 60 .+-. 1.degree. (c 2.0, Me2CO); DL-p-nitro-.alpha.-benzamino, m. 158-9.degree. (cf. S. and I., loc. cit.); D-p-nitro-.alpha.-propionamino (X), m. 134-5.degree., [.alpha.]D -26.5 .+-. 1.degree. (c 4.0, EtOH); DL-p-nitro-.alpha.-propionamino, m. 113-15.degree. (cf. S. and I., loc. cit.); D-p-nitro-.alpha.-chloroacetamino, m. 100-1.degree., [.alpha.]D 6.4 .+-. 1.degree. (c 2.0, EtOH); DL-p-nitro-.alpha.-chloroacetamino, m. 130-1.degree. (cf. S. and I., loc. cit.). The **racemization** of these compds. is exemplified by the following syntheses: VII (1 g.) in 10 cc. C5H5N and 10 cc. NEt3, let stand 3 hrs., poured into ice-HCl, and the product purified by EtOH, give 0.82 g. DL-.alpha.-benzamino-.beta.-hydroxypropiophenone, m.

141-2.degree. (cf. L. and T., loc. cit.). VI (20 g.) in 50 cc. C5H5N (dark red soln.) poured into 200 g. ice and 100 cc. concd. HCl and let stand ppts. 17.2 g. DL-p-nitro-.alpha.-acetamino-.beta.-hydroxypropiophenone (XII), m. 163-4.degree. (cf. L. and T., loc. cit.). A suspension of 20 g. VI in 100 cc. EtOH and 1 g. C5H5N, agitated 90 min., yield 17 g. XII. If, instead, the mixt. is refluxed 1 hr., 12 g. p-nitro-.alpha.-acetaminoacrylophenone, m. 121-2.degree. (cf. A., et al., C.A. 49, 8247d), is obtained. A suspension of 10 g. VI in 100 cc. HNEt2 agitated 10 min. gives 8.8 g. XII. VI (10 g.) in 100 cc. C5H5N let stand 3 days, poured into 300 g. ice and 200 cc. concd. HCl, and let stand gives 7.5 g. XII. A suspension of VI in NEt3 or 1-ethylpiperidine, agitated 4 hrs., and poured into ice-HCl, gives 85% XII. The velocity consts. of the 1st order are detd. by the decrease of rotatory power of 10% C5H5N solns. For the following propiophenones the K values (in hr.-1 .times. 102) and the **acid** dissocn. consts. (.times. 105) of the acylant **acid**, resp., are given: VI, 1.1 .+-. 0.15, 1.82; X, 1.2 .+-. 0.15, 1.34; VIII, 3.1 .+-. 0.1, 6.27; VII, 0, 6.27. These values show the strong influence of the p-NO2 group and the close relation between the energy of the acylant **acid**, NH2 group, and velocity of **racemization**. The K value of XI could not be detd. precisely because of the strong color, but the indications were that it was the highest value of all. The **racemization** of the propiophenones is of importance because of the possibility of utilizing the L-**threo** and D-**erythro** derivs. of phenylaminopropanediol, which heretofore have been waste products in the synthesis of chloroamphenicol. A mechanism is proposed and discussed.

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 12:25:44
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE
100.0% PROCESSED 11 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 21 TO 419
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 ful

FULL SEARCH INITIATED 12:25:54
FULL SCREEN SEARCH COMPLETED - 167 TO ITERATE
100.0% PROCESSED 167 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.01

L3 19 SEA SSS FUL L1

=> fil ca

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	110.32	110.47

FILE 'CA' ENTERED AT 12:26:01 ON 14 OCT 1997
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 14 Oct 1997 (971014/ED) VOL 127 ISS 16

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 42 L3

=> s l4 and threo

6259 THREO
L5 11 L4 AND THREO

=> d 1-11 bib abs

L5 ANSWER 1 OF 11 CA COPYRIGHT 1997 ACS

AN 127:205477 CA
TI Preparation of d- or l-**threo**-methylphenidate by resolution and recycling of undesired enantiomers by epimerization.
IN Langston, Marianne; Zavareh, Hooshang Shahriari
PA Medeva Europe Ltd., UK
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
PI WO 9728124 A1 970807
DS KZ, W MD, W RU, W TJ, W TM, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 97-GB281 970131
PRAI GB 96-2174 960202
GB 96-18836 960910
DT Patent
LA English
AB Title process comprises resoln. of a mixt. of the enantiomers, racemization of the unwanted enantiomer to give a mixt. of all four stereoisomers, and sepn. of the erythro stereoisomers, to leave the **threo** mixt. of enantiomers for resoln. Thus, d-**threo**-methylphenidate was refluxed 4 h with propionic acid in PhMe to give a mixt. of all 4 stereoisomers. Resoln. is carried out using the method of PCT/GB97/00185.

L5 ANSWER 2 OF 11 CA COPYRIGHT 1997 ACS
AN 122:31279 CA
TI Synthesis of the racemate and individual enantiomers of [11C]methylphenidate for studying presynaptic dopaminergic neuron with positron emission tomography
AU Ding, Y.-S.; Sugano, Y.; Fowler, J. S.; Salata, C.
CS Brookhaven National Lab., Upton, NY, 11973, USA
SO J. Labelled Compd. Radiopharm. (1994), 34(10), 989-97
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
AB Carbon-11 labeled dl-**threo**-methylphenidate [i.e., methyl-2-phenyl-2-(2-piperidyl)acetate, Ritalin], a psychostimulant drug widely used to treat attention deficit hyperactivity disorder, was prepd. in two steps: O-methylation of the N-protected DL-**threo**-Ritalin ic acid deriv. with [11C]methyl iodide followed by deprotection. The same strategy was applied for the prepn. of C-11 labeled individual enantiomers of **threo**-methylphenidate from N-protected D-**threo** or L-**threo**-Ritalin ic acid. The subsequent C18 sep-pak and reverse-phase HPLC purifn. resulted in ca. 40% radiochem. yield with a total synthesis time of 40 min and an av. specific activity of 1.5 Ci/.mu.mole (at EOB).

L5 ANSWER 3 OF 11 CA COPYRIGHT 1997 ACS
AN 117:123976 CA
TI Stereoselective urinary pharmacokinetics of dl-**threo**-methylphenidate and its major metabolite in humans
AU Srinivas, N. R.; Hubbard, J. W.; Korchinski, E. D.; Midha, K. K.
CS Coll. Pharm., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SO J. Pharm. Sci. (1992), 81(8), 747-9
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB Stereoselective urinary pharmacokinetics of d,l-**threo**-methylphenidate (MPH) and its major metabolite, d,l-ritalinic acid (RA), were examd. in a cohort of healthy subjects. On two occasions, sepd. by one week, each subject received MPH-HCl either

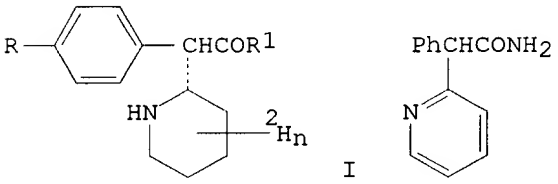
i.v. (10 mg) or orally (40 mg). Urine was collected in six time segments, up to 16 h after each dosing. In the first 2 h after oral administration of MPH, d-MPH found in the urine was 10-fold greater than the l-antipode, whereas there was no significant difference between the amts. of MPH enantiomers excreted after the i.v. dose. Examn. of RA content in the 0-2-h urine samples after oral administration of MPH indicated the presence of higher levels of l-RA (d-RA:l-RA, 0.37), whereas after i.v. MPH, there was no significant difference between the amts. of RA enantiomers. Moreover, after oral administration of MPH, the ratio of d-MPH to l-MPH was .apprx.10 in urine samples from each of the time segments. By contrast, after i.v. administration of MPH, the d:l ratio changed progressively from 1.16 in the 0-2-h urine sample to 9.06 in the 12-16-h sample. These observations suggest that, after oral administration of dl-MPH, the distortion in the ratio of MPH or RA enantiomers in urine samples was attributable to enantioselective presystemic conversion of MPH to RA rather than to enantioselective excretion.

L5 ANSWER 4 OF 11 CA COPYRIGHT 1997 ACS
AN 113:125920 CA
TI Kinetic analysis of enantiomers of **threo**-methylphenidate and its metabolite in two healthy subjects after oral administration as determined by a gas chromatographic-mass spectrometric method
AU Aoyama, Takao; Kotaki, Hajime; Honda, Yutaka; Nakagawa, Fujio
CS Fac. Med., Univ. Tokyo, Tokyo, 113, Japan
SO J. Pharm. Sci. (1990), 79(6), 465-9
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB A gas chromatog.-mass spectrometric method was developed for the stereoselective quantification of **threo**-methylphenidate (MPD) and its metabolite, ritalinic acid (RA), in plasma or urine. The plasma concns. of (+)-MPD after oral administration of two 10-mg conventional tablets contg. racemic MPD-HCl or of 20-mg of racemic MPD-HCl crystals to 2 healthy subjects were much higher than those of the (-)-isomer. The plasma concns. of the metabolite, (-)-RA, were higher than that of the (+)-isomer during the first 4 h after administration of racemic MPD-HCl in both tablet and crystal forms. Although in urine both (+)- and (-)-RA were largely excreted in 48 h (37 and 40% of the dose, resp.), the percentage excretion of (-)-RA during the first 3-4 h was approx. twice that of the (+)-isomer. These results suggest that one reason for the difference in the plasma levels between (+)- and (-)-MPD may be due to differences in their rates of metab. Pharmacokinetic parameters of (+)-MPD after administration of 10 mg of (+)-MPD-HCl crystals were almost the same as those after administration of racemic MPD-HCl crystals. The AUC0.infin. of (-)-MPD after administration of 10 mg of (-)-MPD-HCl crystals was smaller than that after administration of racemic MPD-HCl crystals.

L5 ANSWER 5 OF 11 CA COPYRIGHT 1997 ACS
AN 103:206265 CA
TI [3H]**Threo**-(.+-.)-methylphenidate binding to 3,4-dihydroxyphenylethylamine uptake sites in corpus striatum: correlation with the stimulant properties of ritalinic acid esters
AU Schweri, Margaret M.; Skolnick, Phil; Rafferty, Michael F.; Rice, Kenner C.; Janowsky, Aaron J.; Paul, Steven M.
CS Lab. Bioorg. Chem., NIADDK, Bethesda, MD, 20205, USA
SO J. Neurochem. (1985), 45(4), 1062-70
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
AB Saturable and stereoselective binding sites for 3H-labeled **threo**-(.+-.)-methylphenidate [20748-11-2] were

characterized in rat brain membranes. The highest d. of [3H] **threo**-(.+-.)-methylphenidate binding sites was found in the synaptosomal fraction of corpus striatum. Scatchard anal. revealed a single class of noninteracting binding sites with an apparent dissocn. const. of 235 nM and a max. no. of binding sites of 13.4 pmol/mg protein. Saturable, high-affinity binding of [3H] **threo**-(.+-.)-methylphenidate to striatal synaptosomal membranes was dependent on the presence of Na ions. A good correlation was obsd. between the potencies of various psychotropic drugs in displacing [3H]**threo**-(.+-.)methylphenidate from these sites and their potencies as inhibitors of 3H-labeled 3,4-dihydroxyphenylethylamine (dopamine) [51-61-6] uptake into striatal synaptosomes. A good correlation was also obsd. between the potencies of a series of ritalinic acid esters in inhibiting [3H]**threo**-(.+-.)-methylphenidate binding to striatal synaptosomal membranes and their potencies as motor stimulants in mice. These observations suggest that the binding sites for [3H] **threo**-(.+-.)-methylphenidate described here are assocd. with a dopamine uptake or transport complex, and that these sites may mediate the motor stimulant properties of ritalinic acid esters such as methylphenidate [113-45-1].

L5 ANSWER 6 OF 11 CA COPYRIGHT 1997 ACS
AN 97:144733 CA
TI Synthesis of deuterium-labeled methylphenidate, p-hydroxymethylphenidate, ritalinic acid, and p-hydroxyritalinic acid
AU Patrick, Kennerly; Kilts, Clinton; Breese, George
CS Biol. Sci. Res. Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SO J. Labelled Compd. Radiopharm. (1982), 19(4), 485-90
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
GI

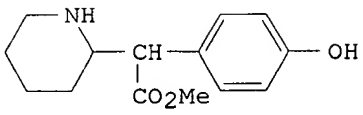


I VI

AB In the prepns. of the title compds. (I; R = H, OH, R1 = OMe; R = H, OH, R1 = OH) (II-V, resp.), all possible combinations of 2H on the piperidine ring were obtained, the most abundant being the pentadeuterated product. Deuteration of the amide VI gave a 70:30 erythro-**threo** mixt. I (R = H, R1 = NH2) which after KOH epimerization and treatment with HCl gave 74% IV.HCl. Subsequent esterification of IV.HCl gave 89% II.HCl. III.HCl and V.HBr were prepd. by modification of a previous method (1981). II-V were prepd. as internal stds. for mass fragmentog. assays of methylphenidate and its metabolites.

L5 ANSWER 7 OF 11 CA COPYRIGHT 1997 ACS
AN 95:125869 CA
TI Synthesis and pharmacology of hydroxylated metabolites of methyl phenidate
AU Patrick, Kennerly S.; Kilts, Clinton D.; Breese, George R.
CS Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SO J. Med. Chem. (1981), 24(10), 1237-40
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal
LA English
GI



I

AB Me **threo**-dl- (I) [78708-74-4] and erythro-dl-p-hydroxymethylphenidate-HCl (II) [78708-67-5] and their resp. deesterified products III [78708-75-5] and IV [78708-76-6] were synthesized and tested for dopaminergic activity in rats. The locomotor response to I was greater than that to II, ritalin (V) [298-59-9], or erythro-dl-methylphenidate-HCl [23644-60-2], suggesting that I may play a role in the pharmacol. of V in the hyperkinetic syndrome in children. **threo**-dl-Ritalinic acid-HBr [**78708-68-6**], erythro-dl-ritalinic acid-HBr [**78779-59-6**], III, and IV produced small increases in locomotor activity relative to their Me esters and the responses were not appreciably affected by stereochem. or para-hydroxylation.

L5 ANSWER 8 OF 11 CA COPYRIGHT 1997 ACS
AN 84:30829 CA
TI New route for synthesis of methyl **threo**-.alpha.-phenyl-.alpha.-(2-piperidyl)acetate hydrochloride
AU Yakhontov, L. N.; Levkoeva, E. I.
CS Vses. Nauchno-Issled. Khim.-Farm. Inst. im. Ordzhonikidze, Moscow, USSR
SO Khim.-Farm. Zh. (1975), 9(10), 19-23
CODEN: KHFZAN
DT Journal
LA Russian
GI For diagram(s), see printed CA Issue.
AB The title compd. I was prepd. in 58% yield by hydrolysis of nitrile II to give the acid which was hydrogenated over an Adams catalyst followed by esterification.

L5 ANSWER 9 OF 11 CA COPYRIGHT 1997 ACS
AN 83:114219 CA
TI Methyl **threo**-.alpha.-phenyl-.alpha.-(2-piperidyl)acetate hydrochloride
IN Yakhontov, L. N.; Levkoeva, E. I.
PA Ordzhonikidze, S., All-Union Scientific-Research Chemical-Pharmaceutical Institute, USSR
SO U.S.S.R.
From: Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki 1975, 52(13), 54.
CODEN: URXXAF
PI SU 466229 750405
AI SU 73-1874299 730123
DT Patent
LA Russian
AB The title phenylpiperidylacetate was prepd. by sapong. .alpha.-phenyl-.alpha.-(2-pyridyl)acetonitrile with aq.-alc. alkali, hydrogenating the resulting salt at 70.degree., 50-60 atm, and pH 7-9 over a Ni catalyst, isomerizing the resulting mixt. of **threo**- and erythro-phenylpiperidylacetate salts by heating in an alk. medium, acidifying to pH 6, and esterifying the resulting **threo**-.alpha.-phenyl-.alpha.-(2-piperidyl)acetic acid.

L5 ANSWER 10 OF 11 CA COPYRIGHT 1997 ACS

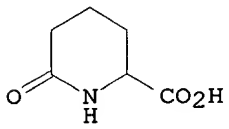
AN 82:118724 CA
TI Metabolism and disposition of methyl phenidate-14C: Studies in man and animals
AU Faraj, B. A.; Israili, Z. H.; Perel, J. M.; Jenkins, M. L.; Holtzman, S. G.; Cucinell, S. A.; Dayton, P. G.
CS Dep. Med., Emory Univ., Atlanta, Ga., USA
SO J. Pharmacol. Exp. Ther. (1974), 191(3), 535-47
CODEN: JPETAB
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB 14C-labeled **threo**-dl-methylphenidate-HCl (**threo**-dl-I-HCl) [23655-65-4] was extensively metab. in man, dog, rat and mouse but with pronounced species differences. In human subjects, blood plasma levels of I were also much higher after i.v. than after oral administration. After oral administration, 50 and 90% of the 14C was excreted in urine in 8 and 48 hrs, resp. This suggests esentially complete absorption of I. The main urinary metabolite was the deesterified product, **threo**-dl-ritalinic acid [**54631-24-2**], accounting for 80% of the dose. Upon i.v. administration of I to dogs, 50-60% of the radioactivity was excreted in 7 hr urine. The major metabolites in dog urine were ritalinic acid and **threo**-dl-2-phenyl-2-(2'-piperidyl-6'-one)acetic acid [54593-31-6]. In rats, both after i.p. and oral administration of I, 50-60% of the 14C was eliminated in urine and 30-40% in feces within 48 hrs. Significant biliary excretion of 14C (25-30% in 12 hrs) was found bile-cannulated rats. The major metabolites in rat urine besides ritalinic acid were **threo**-dl-2-(p-hydroxyphenyl)-2-(2'-piperidyl)acetic acid [54593-32-7], its methyl ester [54593-35-0] and its glucuronide conjugate [54642-79-4]. The locomotor activity of I, certain metabolites and N-acetyl-**threo**-dl-methylphenidate [54593-33-8] was studied in mice.

L5 ANSWER 11 OF 11 CA COPYRIGHT 1997 ACS
AN 70:96027 CA
TI Absolute configurations of the pheniramines, methyl phenidates, and pipradrols
AU Shafi'ee, Abbas; Hite, Gilbert
CS Coll. of Pharm. Sci., Columbia Univ., New York, N. Y., USA
SO J. Med. Chem. (1969), 12(2), 266-70
CODEN: JMCMAR
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Abs. configurations of the 16 optical isomers of seven structurally related title compds. of biol. interest were detd. The pheniramines were converted to a Me phenidate in which the relative configurations of the two asymmetric centers were established. The endocyclic center of asymmetry introduced in the process was maintained intact while the asymmetry of the exocyclic center was destroyed in the conversion to a pipradrol deriv. This was related to pipradrol by an aufbau sequence starting with (R)-(+)-piperidine-2-carboxylic acid. The absolute configurations of deoxypipradrol and thiopipradrol were established by Birch redn. and by rotatory dispersion, resp. The antihistaminically more active acid maleates of Ia and Ib are stereochemically superimposable upon Ic and all have the (S)-configuration. The analeptically more active hydrochlorides of **threo**-Me phenidate, pipradol, and thiopipradrol are stereochemically superimposable upon II. These have the (2R:2'R), (R), (S), and (R) configurations, resp., but are not stereochem. superimposable upon the analeptically more active (+) acid sulfate of amphetamine.

AN 1981:47148 CAPLUS
DN 94:47148
TI **Racemization** of 6-oxo-2-**piperidine-carboxylic acid** enantiomers
IN Miller, Stewart Montague; Nutt, Ruth Foelsche
PA Merck and Co., Inc., USA
SO Brit., 2 pp.
CODEN: BRXXAA
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 1569486	A	19800618	GB 1977-52294	19771215
PRAI US 1976-752934	19761222			

GI



I

AB Either enantiomer of the title compd. I is racemized by heating at 205-50.degree. in an inert atm. Thus, racemic I was resolved into D- and L-I via quinine salts. The sepd. L-I was heated 4 min at 205-50.degree. under N, triturated with EtOH, and dried to give racemic I which was recycled to the resoln. step.